REMARKS

Status of the Claims

Claims 1-3, 5, 6 and 12-19 are currently pending in the application. Claims 1-12 stand rejected. Claims 1, 2, 5, 6 and 12 have been amended as set forth herein. Claims 7-11 have been cancelled herein. All amendments and cancellations are made without prejudice or disclaimer. New claims 13-19 have been added. No new matter has been added by way of the present amendments. Specifically, the amendment to claim 1 is supported by the specification at, for instance, page 1, lines 7-11, page 5, lines 32, to page 6, line 3. The amendments to claims 2 and 6 are merely clarifying amendments. New claims 13-19 are supported in the specification at, for instance, page 9, lines 1-11, page 11, lines 5-9, and pages 15-16. Claims 5 and 12 have been rewritten in independent form for more convenient examination. Reconsideration is respectfully requested.

Information Disclosure Statement

The Examiner states that no indication of the relevance or English language translation of any part of Fujiwara et al. was submitted. However, Fujiwara et al. is in fact listed on the second page of the International Search Report filed in English on May 5, 2005. Fujiwara et al. is listed as an "A" (general state of the art) reference for claims 6-12 and as a "Y" (particular relevance) reference for claims 1-5.

Nonetheless, attached hereto as Appendix A is an English language translation of the relevant parts of Fujiwara et al. Applicants wish to further point out that the spelling of the name

"Fujiwara et al." on the International Search Report is incorrect. In fact, the correct spelling of the name is, "Fujimura et al."

Consideration of the Fujimura et al. reference is respectfully requested.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-6 and 12 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement and written description support in the specification. (*See*, Office Action, at pages 3-14). Applicants traverse the rejection as set forth herein.

Regarding the written description issues, the Examiner states that the specification does not support methods utilizing any GANP gene from any source. Furthermore, the Examiner believes the specification discloses no mutants and therefore the Examiner insists the claims be amended to be directed to only full length GANP.

Regarding enablement, the Examiner states that generating transgenic mammals is highly unpredictable and requires undue experimentation. The Examiner states that Applicants have only shown the ability to generate a transgenic mouse using a mouse GANP gene operably linked to a human Ig enhancer and that this single species is insufficient to enable all possible non-human animal transgenics.

Additionally, the Examiner states that Applicants have failed to show that the method actually produces higher affinity antibodies. The Examiner refers to the Examples wherein a mouse serum is produced containing antibodies that bind to NP, but no data is provided for the degree of affinity of these antibodies or whether these antibodies have higher affinity as compared any other antibody. Finally, the Examiner comments that the transgenic mice claimed

and generated by the methods have no phenotype. The Examiner states that the specification fails to provide any guidance as to how to use such mice that have no phenotype.

Applicants believe that it is clearly within the skill of one of skill in the art to generate mutants and that therefore disclosure of how to generate mutants is not necessary to support the presently claimed invention. Additionally, Applicants insist that generating transgenic animals is routine and well within the skill of one of ordinary skill in the art at the time the present application was filed. The Examiner has provided no evidence to the contrary.

The Examiner is reminded that, "As long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, then the enablement requirement of 35 U.S.C. 112 is satisfied." (*See, In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (CCPA 1970)). Furthermore, Applicants point out that a "patent need not teach, and preferably omits, what is well known in the art." (*See, Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987)).

However, although Applicants do not agree that the presently claimed invention lacks enablement and written description support in the present specification, to expedite prosecution, claim 1 has been amended to recite, in part, "a mouse GANP gene or a human GANP gene."

Therefore, reconsideration and withdrawal of the written description rejection of claims 1-6 and 12 are respectfully requested.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claim 6 stands rejected under 35 U.S.C. § 112, second paragraph, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (*See*, Office Action, at page). Applicants traverse the rejection as set forth herein.

The Examiner believed claim 6 is missing essential steps. However, one of skill in the art certainly knows how to obtain antibodies from a mouse. This is routine procedure to one of skill in the art. Thus, the claim need not recite such limitations. Applicants again respectfully point out to the Examiner that a "patent need not teach, and preferably omits, what is well known in the art." (*See*, *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524, 1534 (Fed. Cir. 1987)). Nevertheless, claim 6 has been amended to include one additional step.

Reconsideration and withdrawal of the indefiniteness rejection of claim 6 are respectfully requested.

Rejections Under 35 U.S.C. § 103(a)

Claims 1-5 stand rejected under 35 U.S.C. § 103(a) as being unpatentable as obvious over Kuwahara et al., *Blood*, 95:2321-2328, 2000 (hereinafter, "Kuwahara et al.") in view of Jaenisch, *Science*, 240:1468-1474, 1988 (hereinafter, "Jaenisch"), and in further view of Maas et al., *J. Immunol.*, 162:6526-6533, 1999 (hereinafter, "Maas et al."). (*See*, Office Action, at pages 15-18). Applicants traverse the rejection as hereinafter set forth.

The Examiner states that Kuwahara et al. disclose that germinal center-associated nuclear protein co-immunoprecipitates with MCM3 in B cells and that GANP is upregulated in differentiated cells and arrests the cell cycle. The Examiner states that Kuwahara et al. posit that "a function of GANP is inactivation of MCM3 by means of binding." (*Id.* at page 16). The

Examiner admits that Kuwahara et al. do not disclose or suggest the *in vivo* role of GANP. The Examiner states that Jaenisch discloses a common method for generating a transgenic mouse using microinjection technology. However, the Examiner admits that Jaenisch do not disclose or suggest a B-cell specific promoter. Finally, the Examiner cites also to Maas et al. for the disclosure of a 6.3 kb genomic fragment with the CD19 promoter which contains a critical B cell-specific activator protein/pax-5 site, allowing generation of transgenic mice that express the gene of interest in only B cells. The Examiner concludes that it would have been obvious to one of ordinary skill in the art to piece together all these disparate elements from all three references.

However, there is no motivation to combine all of these references together to create a transgenic mouse expressing GANP. No two references, when combined, provide the proper motivation to suggest creating such a transgenic mouse or why it would be useful to do so. This is especially true in light of the high degree of unpredictability the Examiner admits is prevalent in the present field of technology.

The "teaching, suggestion, motivation" test is a valid test for obviousness, but one which cannot be too rigidly applied. (*See, KSR International Co. v Teleflex Inc.*, 82 USPQ2d 1385, 1395 (U.S. 2007)). While the courts have adopted a more flexible teaching, suggestion, motivation (TSM) test in connection with the obviousness standard based on the *KSR v. Teleflex* case which involved a mechanical device in a relatively predictable technological area, it remains true that, despite this altered standard, the courts recognize inventors face additional barriers in relatively unpredictable technological areas as noted in *Takeda Chemical Industries, Ltd. v. Alphapharm Pty., Ltd.*, 83 USPQ2d 1169 (Fed. Cir. 2007) (since TSM test can provide helpful insight if it is not applied as rigid and mandatory formula, and since, in cases involving new

chemical compounds, it remains necessary to identify some reason that would have led chemist to modify known compound, in particular manner, in order to establish *prima facie* obviousness of new compound).

The Examiner appears in this instance to be arbitrarily combining completely unrelated references to attempt to establish a *prima facie* case of obviousness. "In determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." *In re Linter*, 458 F.2d 1013, 1016, 173 USPQ 560, 562 (CCPA 1972). References cannot be arbitrarily combined. There must be some reason why one of ordinary skill in the art would be motivated to make the proposed combination of the primary and secondary references. (*See, In re Nomiya*, 184 U.S.P.Q. 607 (C.C.P.A. 1975)).

While patents or references are relevant as prior art for all they contain, they cannot be relied upon to teach embodiments that are not reasonably suggested to one having ordinary skill in the art. (*See, Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804 (Fed. Cir. 1989)). In this regard, such hypothetical embodiments are being generated here to achieve the present invention when the Examiner is taking only pieces of each reference and disregarding other essential disclosures of the references. Thus, the cited references are relevant as prior art for all they contain but at the same time cannot be relied upon to teach embodiments that are not reasonably suggested to one having ordinary skill in the art. (*See, Merck & Co.; supra*).

Finally, Applicants believe the Examiner is clearly utilizing the impermissible practice of hindsight reconstruction in cobbling together the present obviousness rejection. Here, the

Examiner must dissect bits and pieces from each of the three different references, directed to solving different problems, and combine these bits and pieces together in an attempt to create a combination and method similar to that defined by the claims of the present application. Thus, through a process of impermissible hindsight reconstruction, the Examiner is completely reconstructing the teachings of the references in view of the Applicants' own disclosure. (*See, Grain Processing Corp. v. American Maize-Products Co.*, 840 F.2d 902, 907, 5 U.S.P.Q.2d 1788, 1792 (Fed. Cir. 1988), stating "Care must be taken to avoid hindsight reconstruction by using 'the patent in suit as a guide through the maze of prior art references, combining the right references in the right way so as to achieve the result of the claims in suit,'" internal citation omitted; and *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1600 (Fed. Cir. 1988), stating "One cannot use hindsight reconstruction to pick and choose among isolated disclosures in the prior art to deprecate the claimed invention."). The Supreme Court in the *KSR* decision has stated that the "factfinder should be aware, of course, of the distortion caused by hindsight bias." (*See, KSR*, 82 USPQ2d at 1397).

For these reasons, Applicants believe the Examiner has failed to establish a *prima facie* case of obviousness with respect to the presently pending claims.

Reconsideration and withdrawal of the obviousness rejection of claim(s) . . . are respectfully requested.

CONCLUSION

If the Examiner has any questions or comments, please contact Thomas J. Siepmann, Ph.D., Registration No 57,374, at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

Dated: APR 10 2008

Respectfully submitted,

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Attachments: Appendix A – Partial English language translation of Fujimura et al.

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